

Translation

PATENT COOPERATION TREATY

PCT/EP2003/014876



PCT

541 513

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000054221	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/014876	International filing date (day/month/year) 24 December 2003 (24.12.2003)	Priority date (day/month/year) 09 January 2003 (09.01.2003)
International Patent Classification (IPC) or national classification and IPC C12N 9/00, 9/02, C12P 23/00, C12N 5/04		
Applicant BASF AKTIENGESELLSCHAFT		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 01 July 2004 (01.07.2004)	Date of completion of this report 14 April 2005 (14.04.2005)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/014876

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
pages _____ 1-43 _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages _____ 1-43 _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the drawings:
pages _____ 1/3-3/3 _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the sequence listing part of the description:
pages _____ 1-15 _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/014876

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/14876

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

Unity of the invention (PCT Rule 13)

As a result of the assessment of inventive step, the examiner is of the opinion that the claimed subject matter of the present application lacks unity.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/14876

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1-43	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-43	NO
Industrial applicability (IA)	Claims	1-43	YES
	Claims		NO

2. Citations and explanationsThe subject matter of the present application

Method of producing ketocarotinoids by cultivating genetically modified microorganisms or plants with increased ketolase activity characterized in that the modification is brought about by the expression of a ketolase with SEQ. ID. NO. 2 or a ketolase derived therefrom.

Cited documents (PCT Rule 64(1))

D1: EP-A-O 735 137

D2: WO 99/07867 A

D3: WO 99/61652 A

D4: MEEKS ET AL. (2001) PHOTOSYNTHESIS RES. 70, 85-106

D5: WO 03/012056 A

D6: WO 03/080849 A

D7: WO 2004/018693 A

D8: WO 2004/018694 A

D9: DE 102 38 978 A

D10: KANEKO ET AL (2001) DNA RESEARCH 8, 205-213

D11: MOFFITT ET AL. (2003) J. MOL. EVOL. 56, 446-457

D12: MISAWA ET AL. (1998) J. BIOTECHNOL. 59, 169-181

D13: LEE ET AL. (2002) APPL MICROBIOL BIOTECHNOL. 60, 1-11

D14: SIEIRO ET AL (2003) INT. MICROBIOL 6, 11 -16

D15: MISAWA ET AL. (1995) J. BACT. 22, 6575-6584

D5-D9, D11 and D14 are not regarded as prior art under PCT Rule 64(1).

Novelty (PCT Article 33(2))

D1 to D3 and the documents cited on page 3 (lines 1-18) of the description are considered to be the closest prior art. These documents disclose the production of ketocarotenoids using genetically modified organisms (microorganisms and plants) by increasing the ketolase activity. However, the disclosed ketolases have only very little identity with the ketolase of SEQ. ID. NO. 2.

D4 discloses the genomic sequence of the cyanobacteria *Nostoc punctiforme* (see also "<http://genome.ornl.gov/microbial/npun>").

The prior art citations D10 and D11 disclose the sequences of two ketolases (EBI:Q8YSA0 (D10); EBI: Q847D1 (D11)). The ketolase of D10 has an identity of 56% with SEQ. ID. NO. 2 and 59% with SEQ. ID. NO. 4. The presumed ketolase of D11 has an identity of 62% with SEQ. ID. NO. 2 and 79% with SEQ. ID. No. 4.

D12-D14 describe the production of carotenoids using genetically modified microorganisms.

Conclusion: The subject matter of claims 1 to 43 is novel.

Inventive step (PCT Article 33(3))

The closest prior art is D1 to D3.

Thus the problem to be solved by the present application can be regarded as that of providing an alternative ketolase.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/14876

The applicant's solution for providing a ketolase with SEQ. ID. NO. 2 or a ketolase derived therefrom currently does not appear to be inventive for two reasons.

- 1) The examiner is of the opinion that **any** ketolase solves the problem. In light of the fact that: i) it was known that some cyanobacteria synthesize ketocarotenoids, and ii) the genomic sequence of one of these cyanobacteria was known, it was obvious for a person skilled in the art to identify sequences from these cyanobacteria which are homologous with crtW or crtO and to use them as alternatives. Consequently, an inventive step could be recognized only if direct comparative experiments were provided and unexpected effects present.
- 2) The lower limit of the identity of the derived ketolases (42%) appears to be selected only to: i) establish novelty over, for example, crtW or crtO, and ii) establish unity between SEQ. ID. NO. 2 and 4 (53% identical), but not to support experimental values. Consequently, this feature cannot be taken into account for the assessment of inventive step. Since this is apparently a new group of ketolases, a lower identity limit of 70-75% would appear to be acceptable.

The additional features in the dependent claims are known to a person skilled in the art.

An inventive step therefore currently cannot be recognized for claims 1 to 43.

Industrial applicability (PCT Article 33(4))

The subject matter of claims 1 to 43 is industrially applicable.